

10/629,749

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	123	(anhydroecgonine or methylecgonidine or anhydromethylecgonine)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 15:17
L2	2	l1 same antibod?	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 14:23
L3	208	(anhydroecgonine or methylecgonidine or anhydromethylecgonine or ecgonidine)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 15:22
L4	17	l3 and antibod?	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 14:23
L5	20	l3 and antibod\$3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 14:24
L6	2	l1 same antibod\$3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 14:23
L7	98	crack adj cocaine	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 14:42
L8	48	l7 same antibod\$3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 14:24

EAST Search History

L9	7	l8 and monoclonal	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 14:25
L10	11	l7 and immunoassay\$1	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 15:05
L11	235	cocaine adj metabolite\$1	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 15:05
L12	165	l11 and antibod\$3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 15:06
L13	73	l11 same antibod\$3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 15:06
L14	2	anhydroecgonine same antibod\$3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 15:19
L15	2	ecgonidine same antibod\$3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 15:18
L16	1	ecgonidine near3 antibod\$3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 15:19

EAST Search History

L17	2	anhydroecgonine near3 antibod\$3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 15:19
L18	2	"20020177714"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 15:25
L19	2	"20050026303"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 15:27
L20	2	("5376667").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2006/06/06 16:00
L21	126	monoclonal adj antibod\$3 same cocaine	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 16:01
L22	2	l21 and (ecgonidine or methylecgonidine or anhydroecgonine)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 16:04
L23	109	(ecgonidine or methylecgonidine or anhydroecgonine or anhydromethylecgonine) and (immunogen or hapten or carrier or BSA or KHL or albumin or globulin)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 16:16
L24	0	(ecgonidine or methylecgonidine or anhydroecgonine or anhydromethylecgonine) same (immunogen or hapten or carrier or BSA or KHL or albumin or globulin)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 16:06

EAST Search History

L25	0	(ecgonidine or methylecgonidine or anhydroecgonine or anhydromethylecgonine) near5 (immunogen or hapten or carrier or BSA or KHL or albumin or globulin)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 16:07
L26	9	I23 and monoclonal	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 16:07
L27	112	(ecgonidine or methylecgonidine or anhydroecgonine or anhydromethylecgonine) and (immunogen or conjugate or hapten or carrier or BSA or KHL or albumin or globulin)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 16:16
L28	9	I27 and monoclonal	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 16:31
L29	2	("5821249").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2006/06/06 16:17
L30	1	natalie near1 lu and monoclonal	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 16:32
L31	1	natalie near1 lu and cocaine	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 16:33
L32	1	(anhydroecgonine and ecgonidine and monoclonal and immunogen and carrier and BSA and KLH and ovalbumin and albumin).clm.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 16:35

EAST Search History

L33	1	(anhydroecgonine and ecgonidine and monoclonal).clm.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 16:35
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10/627,749

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NEWS 7 FEB 27 New STN AnaVist pricing effective March 1, 2006
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NEWS 10 APR 03 New IPC 8 fields and IPC thesaurus added to PATDPAFULL
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thesaurus added in PCTFULL
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NEWS 14 APR 12 Improved structure highlighting in FQHIT and QHIT display
in MARPAT
NEWS 15 APR 12 Derwent World Patents Index to be reloaded and enhanced during
second quarter; strategies may be affected
NEWS 16 MAY 10 CA/CAPLUS enhanced with 1900-1906 U.S. patent records
NEWS 17 MAY 11 KOREAPAT updates resume
NEWS 18 MAY 19 Derwent World Patents Index to be reloaded and enhanced
NEWS 19 MAY 30 IPC 8 Rolled-up Core codes added to CA/CAPLUS and
USPATFULL/USPAT2
NEWS 20 MAY 30 The F-Term thesaurus is now available in CA/CAPLUS
NEWS 21 JUN 02 The first reclassification of IPC codes now complete in
INPADOC

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SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

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=> s (anhydroecgonine or ecgonidine or methylecgonidine or andydromethylecgonine)

144 ANHYDROECGONINE

2 ANHYDROECGONINES

144 ANHYDROECGONINE

(ANHYDROECGONINE OR ANHYDROECGONINES)

60 ECGONIDINE

38 METHYLECGONIDINE

1 METHYLECGONIDINES

38 METHYLECGONIDINE

(METHYLECGONIDINE OR METHYLECGONIDINES)

0 ANDYDROMETHYLECGONINE

L1 211 (ANHYDROECGONINE OR ECGONIDINE OR METHYLECGONIDINE OR ANDYDROMETHYLECGONINE)

=> s l1 and antibod?

462722 ANTIBOD?

L2

3 L1 AND ANTIBOD?

=> d l2 ibib abs hitstr tot

L2 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:99022 CAPLUS

DOCUMENT NUMBER: 142:171445

TITLE: Monoclonal **antibodies** specific for crack cocaine metabolites, a cell line producing the same, and crack cocaine conjugates

INVENTOR(S): Lu, Natalie T.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 8 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 2005026303	A1	20050203	US 2003-629749	20030730
PRIORITY APPLN. INFO.:			US 2003-629749	20030730

AB A monoclonal **antibody**, and a cell line capable of producing the same, has been produced with the ability to detect the primary metabolites generated from the pyrolysis of smokeable, or "crack", cocaine. This monoclonal **antibody**, while being highly specific for **anhydroecgonine** Me ester (AEME) and **ecgonidine** (ECD), does not cross-react at a significant level with the primary cocaine metabolites of powdered or injected cocaine. Crack cocaine metabolite-protein conjugates with or without linkers are used to immunize animals for the production of monoclonal **antibodies**. The **antibodies** can be used in immunoassays to discriminate between the use of crack cocaine and the powdered or injected forms.

L2 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:957786 CAPLUS

DOCUMENT NUMBER: 140:138736

TITLE: Three-Dimensional Quantitative Structure-Activity Relationship Modeling of Cocaine Binding by a Novel Human Monoclonal **Antibody**

AUTHOR(S): Paula, Stefan; Tabet, Michael R.; Farr, Carol D.; Norman, Andrew B.; Ball, W. James, Jr.

CORPORATE SOURCE: College of Medicine, Department of Pharmacology and Cell Biophysics, University of Cincinnati, Cincinnati, OH, 45267-0575, USA

SOURCE: Journal of Medicinal Chemistry (2004), 47(1), 133-142
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Human monoclonal **antibodies** (mAbs) designed for immunotherapy have a high potential for avoiding the complications that may result from human immune system responses to the introduction of nonhuman mAbs into patients. This study presents a characterization of cocaine/**antibody** interactions that determine the binding properties of the novel human sequence mAb 2E2 using three-dimensional quant. structure-activity relationship (3D-QSAR) methodol. We have exptl. determined the binding affinities of mAb 2E2 for cocaine and 38 cocaine analogs. The Kd of mAb 2E2 for cocaine was 4 nM, indicating a high affinity. Also, mAb 2E2 displayed good cocaine specificity, as reflected in its 10-, 1500-, and 25000-fold lower binding affinities for the three physiol. relevant cocaine metabolites benzoylecgonine, ecgonine Me ester, and ecgonine, resp. 3D-QSAR models of cocaine binding were developed by comparative mol. similarity index anal. (CoMSIA). A model of high statistical quality was generated showing that cocaine binds to mAb 2E2 in a sterically restricted binding site that leaves the Me group attached to the ring nitrogen of cocaine solvent-exposed. The Me ester group of cocaine appears to engage in attractive van der Waals interactions with mAb 2E2, whereas the Ph group contributes to the binding primarily via hydrophobic interactions. The model further indicated that an increase in partial pos. charge near the nitrogen proton and Me ester carbonyl group enhances binding affinity and that the ester oxygen likely forms an intermol. hydrogen bond with mAb 2E2. Overall, the cocaine binding properties of mAb 2E2 support its clin. potential for development as a treatment of cocaine overdose and addiction.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:182723 CAPLUS

DOCUMENT NUMBER: 136:386282

TITLE: Synthesis, Properties, and Reactivity of Cocaine Benzoylthio Ester Possessing the Cocaine Absolute Configuration

AUTHOR(S): Isomura, Shigeki; Hoffman, Timothy Z.; Wirsching, Peter; Janda, Kim D.

CORPORATE SOURCE: Department of Chemistry BCC-582, The Scripps Research Institute, La Jolla, CA, 92037, USA

SOURCE: Journal of the American Chemical Society (2002), 124(14), 3661-3668
CODEN: JACSAT; ISSN: 0002-7863

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 136:386282

AB One aspect of immunopharmacotherapy for cocaine abuse involves the use of a catalytic monoclonal **antibody** (mAb) to degrade cocaine via hydrolysis of the benzoate ester. A cocaine benzoylthio ester analog provides a means to implement high-throughput selection strategies to potentially isolate mAbs with high activity. The required analog was synthesized starting from (-)-cocaine hydrochloride and possessed the cocaine absolute configuration. Key points in the preparation were the introduction of the sulfur atom at C-3 via a bromomagnesium thiolate addition to the exo face of **anhydroecgonine**, separation of C-2 diastereomers, recycling of a C-2 thio ester byproduct, and formation of the necessary C-2 Me and C-3 benzoylthio esters. Effects resulting from the lower electronegativity and greater hydrophobicity of sulfur compared to oxygen were observed. These characteristics could result in interesting drug properties. Furthermore, the analog was found to be a substrate for catalytic mAbs that hydrolyze cocaine as monitored by HPLC and also spectrophotometry by coupling cleavage of the benzoylthio ester to the disulfide exchange with Ellman's reagent. Screening **antibody** libraries with the new cocaine analog using the spectroscopic assay provides an avenue for the high-throughput identification of catalysts that efficiently breakdown cocaine.

REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s crack cocaine
108011 CRACK
59042 CRACKS
142529 CRACK
(CRACK OR CRACKS)
19976 COCAINE
45 COCAINES
19981 COCAINE
(COCAINE OR COCAINES)

L3 67 CRACK COCAINE
(CRACK(W) COCAINE)

=> s l3 and antibod?
462722 ANTIBOD?

L4 3 L3 AND ANTIBOD?

=> s l4 not l2
L5 2 L4 NOT L2

=> d l5 ibib abs hitstr tot

L5 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:391023 CAPLUS

TITLE: Risk factors for Kaposi's sarcoma among HHV-8 seropositive homosexual men with AIDS

AUTHOR(S): Nawar, Eric; Mbulaiteye, Sam M.; Gallant, Joel E.; Wohl, David A.; Ardini, Marianne; Hendershot, Tabitha;

CORPORATE SOURCE: Goedert, James J.; Rabkin, Charles S.
The AIDS Cancer Cohort ACC Study Collaborators,
Division of Cancer Epidemiology and Genetics, National
Cancer Institute, Department of Health and Human
Services, National Institutes of Health, Bethesda, MD,
USA
SOURCE: International Journal of Cancer (2005), 115(2),
296-300
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Kaposi's sarcoma (KS) is a frequent complication of the acquired immunodeficiency syndrome (AIDS) in homosexual men. Risk factors for developing this malignancy are uncertain, other than immunosuppression and coinfection with human herpesvirus 8 (HHV-8). We therefore examined factors associated with KS in a cross-sectional anal. of 99 cases among 503 HHV-8 seropos. homosexual men with AIDS. Data were collected by computer-assisted personal interviews and medical chart reviews. HHV-8 seroreactivity was determined by ELISA for **antibodies** against HHV-8 K8.1 glycoprotein. KS was significantly less common in blacks compared to whites [risk ratio (RR) = 0.4; 95% CI = 0.2-0.8] and more common in subjects who had completed college (RR = 1.7; 95% CI = 1.1-2.7) or had annual income greater than \$30,000 (RR = 1.5; 95% CI = 1.1-2.2). KS was less common in cigarette smokers (RR = 0.6; 95% CI = 0.5-0.9) and users of **crack cocaine** (RR = 0.4; 95% CI = 0.1-0.8). KS was less common in bisexual men compared to men who were exclusively homosexual (estimated RR = 0.6; 95% CI = 0.4-0.9) and inversely associated with number of female partners. KS was also less common in men who had received pay for sex (RR = 0.6; 95% CI = 0.4-1.0). These cross-sectional assocns. could be biased by potential differences in relative timing of HHV-8 and HIV infection, a postulated determinant of KS risk. Alternatively, our findings may reflect factors protective against KS in individuals infected with HHV-8. Future research should focus on identifying practical measures for countering KS that do not increase the risk of other diseases.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:237608 CAPLUS

DOCUMENT NUMBER: 126:259082

TITLE: Acute activation of circulating polymorphonuclear neutrophils following in vivo administration of cocaine. A potential etiology for pulmonary injury
AUTHOR(S): Baldwin, Gayle Cocita; Buckley, Dawn M.; Roth, Michael D.; Kleerup, Eric C.; Tashkin, Donald P.

CORPORATE SOURCE: Divisions of Hematology-Oncology and Pulmonary and Critical Care, Department of Medicine, UCLA School of Medicine, Los Angeles, CA, 90095-1678, USA

SOURCE: Chest (1997), 111(3), 698-705
CODEN: CHETBF; ISSN: 0012-3692

PUBLISHER: American College of Chest Physicians

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Crack cocaine** has become a major drug of abuse in the United States and its use is associated with a broad spectrum of pulmonary complications. The present study was conducted to determine whether controlled in vivo administration of cocaine (inhaled or IV) alters the function of circulating inflammatory cells in a manner capable of contributing to acute lung injury. Subjects who regularly smoked **crack cocaine** were asked to abstain from illicit drug use for at least 8 h, and were then administered one of the following treatments on each of 4 study days: inhaled cocaine base (45 mg), inhaled placebo (4.5 mg cocaine base, a subphysiol. dose), IV cocaine HCl (0.35 to 0.50 mg/kg), or IV

placebo (saline solution). Samples of blood were obtained from a peripheral venous catheter and blood cells were isolated before and 10 to 45 min after treatment. The administration of either cocaine base or cocaine HCl, but not their corresponding placebos, resulted in the activation of circulating polymorphonuclear neutrophils (PMNs). Exposure to cocaine in vivo enhanced the antibacterial activity of PMNs, as measured by their ability to kill *Staphylococcus aureus*. Antitumor activity, as measured in an **antibody**-dependent cell-mediated cytotoxicity assay, also increased following short-term administration of cocaine. Finally, short-term exposure to cocaine enhanced production of interleukin 8, a potent PMN chemoattractant and neutrophil-activating factor associated with both acute and chronic lung injury. These studies demonstrate that short-term in vivo exposure to cocaine activates the effector function and cytokine production of circulating PMNs. Therefore, it is possible that bursts of acute inflammatory activity resulting from crack use could contribute to lung injury.

=> s (anhydroecgonine or ecgonidine or methylecgonidine or andydromethylecgonine or crack cocaine)

```

144 ANHYDROECGONINE
  2 ANHYDROECGONINES
144 ANHYDROECGONINE
    (ANHYDROECGONINE OR ANHYDROECGONINES)
 60 ECGONIDINE
 38 METHYLECGONIDINE
  1 METHYLECGONIDINES
 38 METHYLECGONIDINE
    (METHYLECGONIDINE OR METHYLECGONIDINES)
  0 ANDYDROMETHYLECGONINE
108011 CRACK
 59042 CRACKS
142529 CRACK
    (CRACK OR CRACKS)
19976 COCAINE
  45 COCAINES
19981 COCAINE
    (COCAINE OR COCAINES)
 67 CRACK COCAINE
    (CRACK(W) COCAINE)
L6      264 (ANHYDROECGONINE OR ECGONIDINE OR METHYLECGONIDINE OR ANDYDROMET
        HYLECGONINE OR CRACK COCAINE)

```

=> s 16 and immunoassy?

```

31 IMMUNOASSY?
L7      0 L6 AND IMMUNOASSY?

```

=> s 16 and monoclonal

```

139709 MONOCLONAL
 525 MONOCLONALS
139770 MONOCLONAL
    (MONOCLONAL OR MONOCLONALS)
L8      3 L6 AND MONOCLONAL

```

=> s 18 not 15 12

MISSING OPERATOR L5 L2

The search profile that was entered contains terms or nested terms that are not separated by a logical operator.

=> s 18 not 15

```

L9      3 L8 NOT L5

```

=> s 19 not 12

```

L10     0 L9 NOT L2

```

=> cocaine and monoclonal
 COCAINE IS NOT A RECOGNIZED COMMAND
 The previous command name entered was not recognized by the system.
 For a list of commands available to you in the current file, enter
 "HELP COMMANDS" at an arrow prompt (=>).

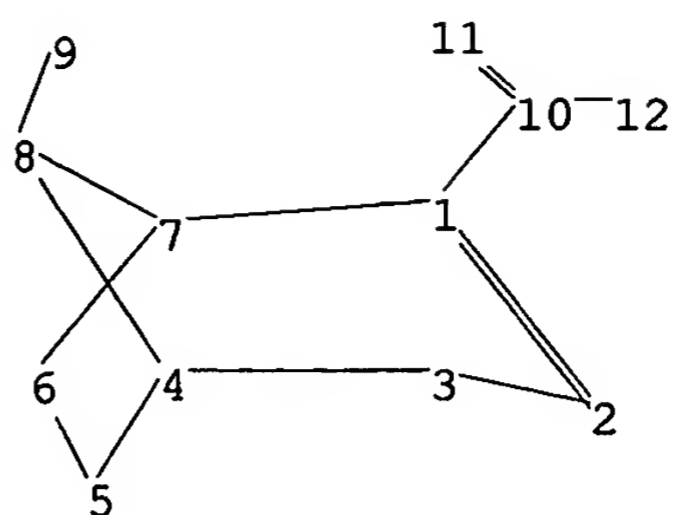
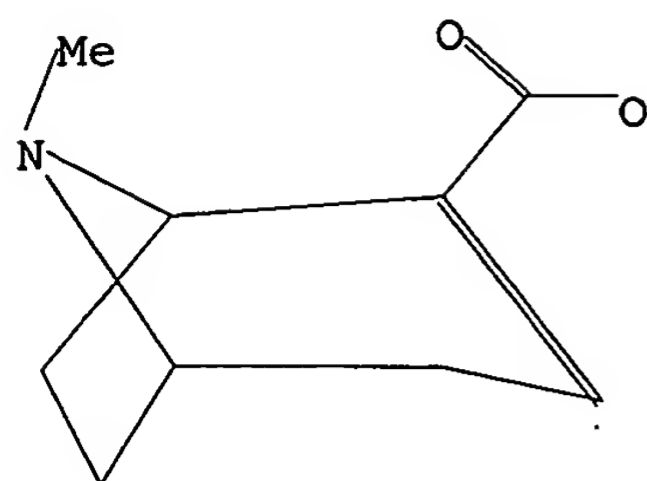
=> s cocaine and monoclonal
 19976 COCAINE
 45 COCAINES
 19981 COCAINE
 (COCAINE OR COCAINES)
 139709 MONOCLONAL
 525 MONOCLONALS
 139770 MONOCLONAL
 (MONOCLONAL OR MONOCLONALS)
 L11 134 COCAINE AND MONOCLONAL

=> s l11 and (AEME or ECD or ecgonidine or anhydroecgonine or methylecgonidine or
 anhydromethylecgonine)
 26 AEME
 4705 ECD
 142 ECDS
 4766 ECD
 (ECD OR ECDS)
 60 ECGONIDINE
 144 ANHYDROECGONINE
 2 ANHYDROECGONINES
 144 ANHYDROECGONINE
 (ANHYDROECGONINE OR ANHYDROECGONINES)
 38 METHYLECGONIDINE
 1 METHYLECGONIDINES
 38 METHYLECGONIDINE
 (METHYLECGONIDINE OR METHYLECGONIDINES)
 0 ANHYDROMETHYLECGONINE
 L12 3 L11 AND (AEME OR ECD OR ECGONIDINE OR ANHYDROECGONINE OR METHYLE
 CGONIDINE OR ANHYDROMETHYLECGONINE)

=> s l12 not l2
 L13 0 L12 NOT L2

=> log y		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	77.98	78.19
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-3.75	-3.75

STN INTERNATIONAL LOGOFF AT 15:15:21 ON 06 JUN 2006



```

chain nodes :
9 10 11 12
ring nodes :
1 2 3 4 5 6 7 8
chain bonds :
1-10 8-9 10-11 10-12
ring bonds :
1-2 1-7 2-3 3-4 4-5 4-8 5-6 6-7 7-8
exact/norm bonds :
1-2 1-7 2-3 3-4 4-8 7-8 10-11 10-12
exact bonds :
1-10 4-5 5-6 6-7 8-9
isolated ring systems :
containing 1 :

```

```

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:CLASS 10:CLASS
11:CLASS 12:CLASS

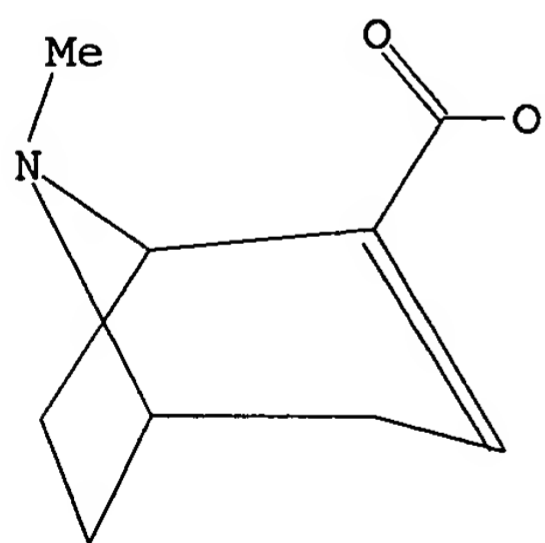
```

L1 STRUCTURE UPLOADED

```

=> d 11
L1 HAS NO ANSWERS
L1 STR

```



Structure attributes must be viewed using STN Express query preparation.

```

=> s 11
SAMPLE SEARCH INITIATED 08:04:23 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 263 TO ITERATE

```

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100.0% PROCESSED 263 ITERATIONS
SEARCH TIME: 00.00.01

```

8 ANSWERS

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 4287 TO 6233
PROJECTED ANSWERS: 8 TO 329

L2 8 SEA SSS SAM L1

=> s 11 sss full

FULL SEARCH INITIATED 08:04:31 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 4919 TO ITERATE

100.0% PROCESSED 4919 ITERATIONS
SEARCH TIME: 00.00.01

160 ANSWERS

L3 160 SEA SSS FUL L1

=> FIL CAPLUS

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

166.94

167.15

FILE 'CAPLUS' ENTERED AT 08:04:37 ON 07 JUN 2006

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FILE LAST UPDATED: 6 Jun 2006 (20060606/ED)

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=> s 13

L4 266 L3

=> s 13 and antibod?

266 L3

462814 ANTIBOD?

L5 6 L3 AND ANTIBOD?

=> s 13 and monoclonal

266 L3

139728 MONOCLONAL

525 MONOCLONALS

139789 MONOCLONAL

(MONOCLONAL OR MONOCLONALS)

L6 4 L3 AND MONOCLONAL

=> s 14 and monoclonal

139728 MONOCLONAL

525 MONOCLONALS
139789 MONOCLONAL
(MONOCLONAL OR MONOCLONALS)
L7 4 L4 AND MONOCLONAL

=> dup rem 15 17
PROCESSING COMPLETED FOR L5
PROCESSING COMPLETED FOR L7
L8 6 DUP REM L5 L7 (4 DUPLICATES REMOVED)
ANSWERS '1-6' FROM FILE CAPLUS

=> s 14 and (immunogen or hapten or conjugate)
6256 IMMUNOGEN
3508 IMMUNOGENS
8742 IMMUNOGEN
(IMMUNOGEN OR IMMUNOGENS)
9760 HAPTEN
6712 HAPTENS
12327 HAPTEN
(HAPTEN OR HAPTENS)
64873 CONJUGATE
57977 CONJUGATES
100624 CONJUGATE
(CONJUGATE OR CONJUGATES)
L9 14 L4 AND (IMMUNOGEN OR HAPTEN OR CONJUGATE)

=> s 19 not 18
L10 6 S L8
L11 11 L9 NOT L10

=> d 18 ibib abs hitstr tot

L8 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2005:99022 CAPLUS
DOCUMENT NUMBER: 142:171445
TITLE: Monoclonal **antibodies** specific for crack cocaine metabolites, a cell line producing the same, and crack cocaine conjugates
INVENTOR(S): Lu, Natalie T.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005026303	A1	20050203	US 2003-629749	20030730
PRIORITY APPLN. INFO.:			US 2003-629749	20030730

AB A monoclonal **antibody**, and a cell line capable of producing the same, has been produced with the ability to detect the primary metabolites generated from the pyrolysis of smokeable, or "crack", cocaine. This monoclonal **antibody**, while being highly specific for anhydroecgonine Me ester (AEME) and ecgonidine (ECD), does not cross-react at a significant level with the primary cocaine metabolites of powdered or injected cocaine. Crack cocaine metabolite-protein conjugates with or without linkers are used to immunize animals for the production of monoclonal **antibodies**. The **antibodies** can be used in immunoassays to discriminate between the use of crack cocaine and the powdered or injected forms.

IT 484-93-5, Ecgonidine 43021-26-7, Anhydroecgonine methyl

ester

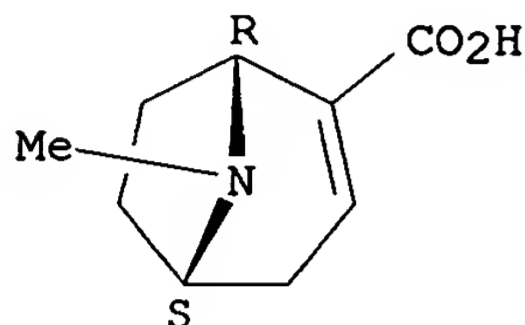
RL: ANT (Analyte); ANST (Analytical study)

(monoclonal **antibodies** specific for crack cocaine metabolites
for use in immunoassays)

RN 484-93-5 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, (1R,5S)- (9CI)
(CA INDEX NAME)

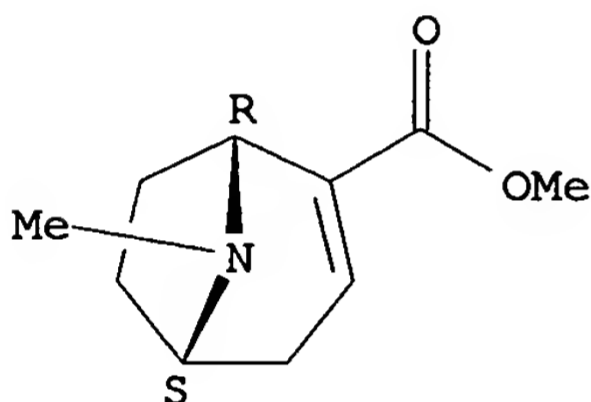
Absolute stereochemistry. Rotation (-).



RN 43021-26-7 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, methyl ester,
(1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



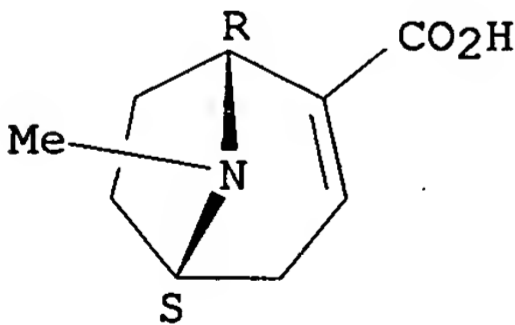
IT **484-93-5D**, Ecgonidine, protein conjugates **43021-26-7D**,
Anhydroecgonine methyl ester, protein conjugates

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(monoclonal **antibodies** specific for crack cocaine metabolites
for use in immunoassays)

RN 484-93-5 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, (1R,5S)- (9CI)
(CA INDEX NAME)

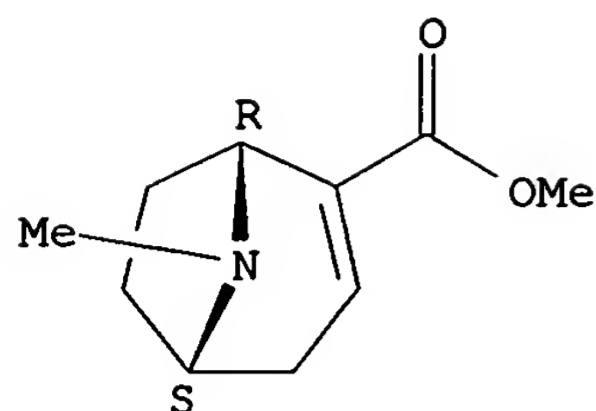
Absolute stereochemistry. Rotation (-).



RN 43021-26-7 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, methyl ester,
(1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2
 ACCESSION NUMBER: 2003:957786 CAPLUS
 DOCUMENT NUMBER: 140:138736
 TITLE: Three-Dimensional Quantitative Structure-Activity Relationship Modeling of Cocaine Binding by a Novel Human Monoclonal **Antibody**
 AUTHOR(S): Paula, Stefan; Tabet, Michael R.; Farr, Carol D.; Norman, Andrew B.; Ball, W. James, Jr.
 CORPORATE SOURCE: College of Medicine, Department of Pharmacology and Cell Biophysics, University of Cincinnati, Cincinnati, OH, 45267-0575, USA
 SOURCE: Journal of Medicinal Chemistry (2004), 47(1), 133-142
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English

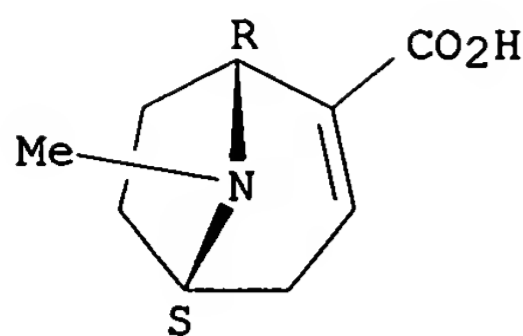
AB Human monoclonal **antibodies** (mAbs) designed for immunotherapy have a high potential for avoiding the complications that may result from human immune system responses to the introduction of nonhuman mAbs into patients. This study presents a characterization of cocaine/**antibody** interactions that determine the binding properties of the novel human sequence mAb 2E2 using three-dimensional quant. structure-activity relationship (3D-QSAR) methodol. We have exptl. determined the binding affinities of mAb 2E2 for cocaine and 38 cocaine analogs. The Kd of mAb 2E2 for cocaine was 4 nM, indicating a high affinity. Also, mAb 2E2 displayed good cocaine specificity, as reflected in its 10-, 1500-, and 25000-fold lower binding affinities for the three physiol. relevant cocaine metabolites benzoylecgonine, ecgonine Me ester, and ecgonine, resp. 3D-QSAR models of cocaine binding were developed by comparative mol. similarity index anal. (CoMSIA). A model of high statistical quality was generated showing that cocaine binds to mAb 2E2 in a sterically restricted binding site that leaves the Me group attached to the ring nitrogen of cocaine solvent-exposed. The Me ester group of cocaine appears to engage in attractive van der Waals interactions with mAb 2E2, whereas the Ph group contributes to the binding primarily via hydrophobic interactions. The model further indicated that an increase in partial pos. charge near the nitrogen proton and Me ester carbonyl group enhances binding affinity and that the ester oxygen likely forms an intermol. hydrogen bond with mAb 2E2. Overall, the cocaine binding properties of mAb 2E2 support its clin. potential for development as a treatment of cocaine overdose and addiction.

IT **484-93-5, Ecgonidine**
 RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
 (three-dimensional quant. structure-activity relationship modeling of cocaine binding by a novel human monoclonal **antibody**)

RN 484-93-5 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, (1R,5S)- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3
 ACCESSION NUMBER: 2002:182723 CAPLUS
 DOCUMENT NUMBER: 136:386282
 TITLE: Synthesis, Properties, and Reactivity of Cocaine Benzoylthio Ester Possessing the Cocaine Absolute Configuration
 AUTHOR(S): Isomura, Shigeki; Hoffman, Timothy Z.; Wirsching, Peter; Janda, Kim D.
 CORPORATE SOURCE: Department of Chemistry BCC-582, The Scripps Research Institute, La Jolla, CA, 92037, USA
 SOURCE: Journal of the American Chemical Society (2002), 124(14), 3661-3668
 CODEN: JACSAT; ISSN: 0002-7863
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 136:386282

AB One aspect of immunopharmacotherapy for cocaine abuse involves the use of a catalytic monoclonal **antibody** (mAb) to degrade cocaine via hydrolysis of the benzoate ester. A cocaine benzoylthio ester analog provides a means to implement high-throughput selection strategies to potentially isolate mAbs with high activity. The required analog was synthesized starting from (-)-cocaine hydrochloride and possessed the cocaine absolute configuration. Key points in the preparation were the introduction of the sulfur atom at C-3 via a bromomagnesium thiolate addition to the exo face of anhydroecgonine, separation of C-2 diastereomers, recycling of a C-2 thio ester byproduct, and formation of the necessary C-2 Me and C-3 benzoylthio esters. Effects resulting from the lower electronegativity and greater hydrophobicity of sulfur compared to oxygen were observed. These characteristics could result in interesting drug properties. Furthermore, the analog was found to be a substrate for catalytic mAbs that hydrolyze cocaine as monitored by HPLC and also spectrophotometry by coupling cleavage of the benzoylthio ester to the disulfide exchange with Ellman's reagent. Screening **antibody** libraries with the new cocaine analog using the spectroscopic assay provides an avenue for the high-throughput identification of catalysts that efficiently breakdown cocaine.

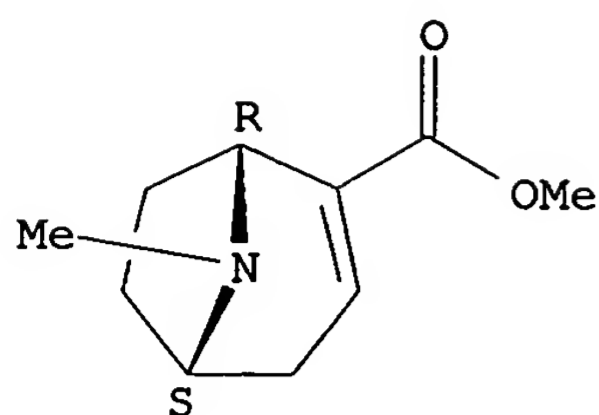
IT 43021-26-7

RL: RCT (Reactant); RACT (Reactant or reagent)
 (synthesis of a cocaine benzoylthio ester analog possessing the cocaine absolute configuration and evaluation of it as a substrate for cocaine hydrolyzing catalytic monoclonal **antibodies**)

RN 43021-26-7 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, methyl ester, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 168143-65-5P 426813-48-1P

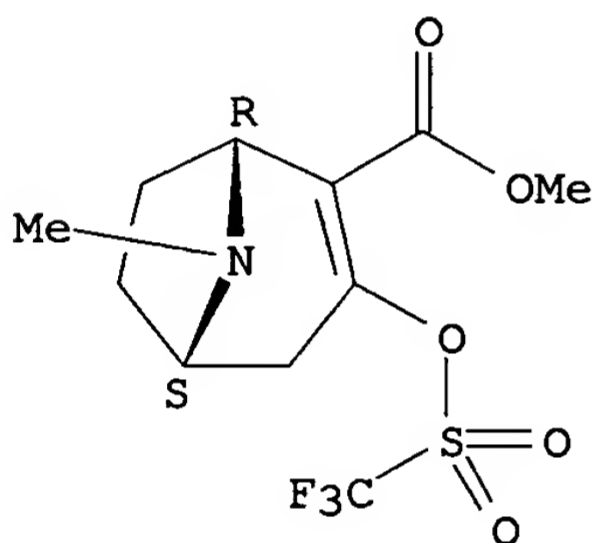
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis of a cocaine benzoylthio ester analog possessing the cocaine absolute configuration and evaluation of it as a substrate for cocaine hydrolyzing catalytic monoclonal **antibodies**)

RN 168143-65-5 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-3-[[trifluoromethylsulfonyl]oxy]-, methyl ester, (1R,5S)- (9CI) (CA INDEX NAME)

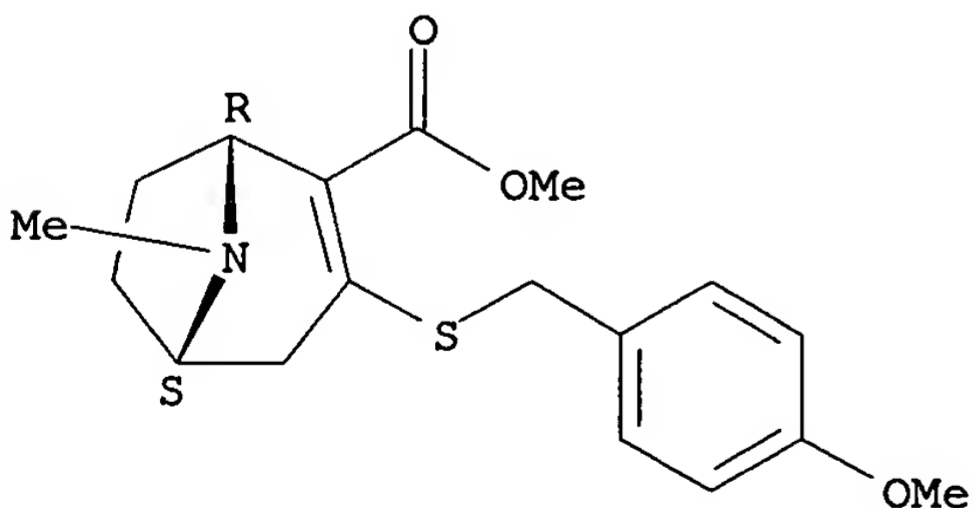
Absolute stereochemistry. Rotation (+).



RN 426813-48-1 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 3-[[[4-methoxyphenyl)methyl]thio]-8-methyl-, methyl ester, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 426813-47-0P 426813-50-5P

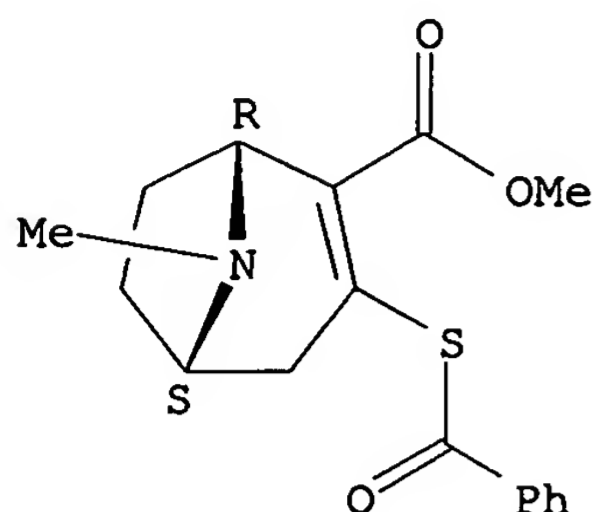
RL: SPN (Synthetic preparation); PREP (Preparation)

(synthesis of a cocaine benzoylthio ester analog possessing the cocaine absolute configuration and evaluation of it as a substrate for cocaine hydrolyzing catalytic monoclonal **antibodies**)

RN 426813-47-0 CAPLUS

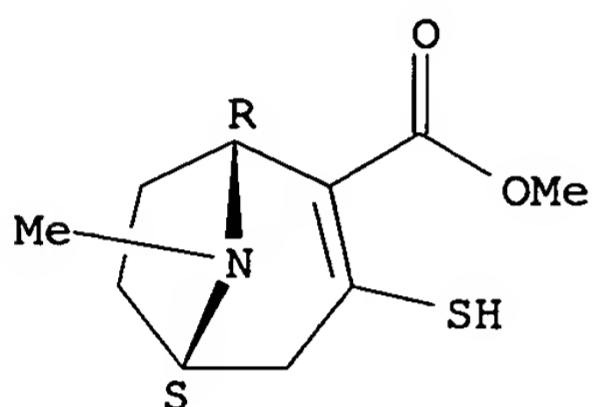
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 3-(benzoylthio)-8-methyl-, methyl ester, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 426813-50-5 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 3-mercapto-8-methyl-,
methyl ester, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

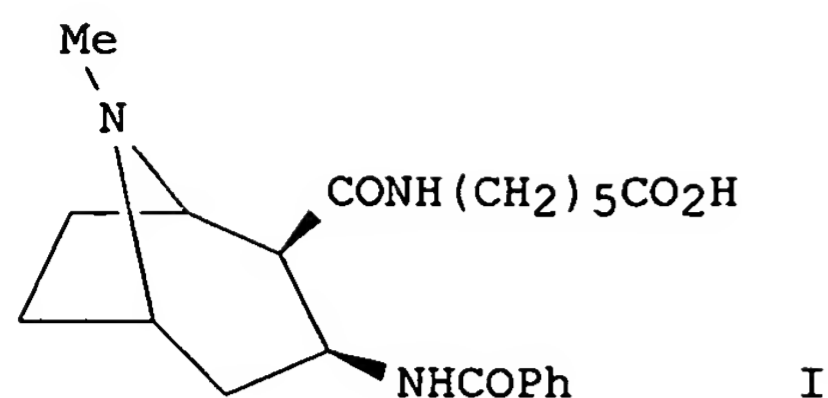


REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 1997:516313 CAPLUS
DOCUMENT NUMBER: 127:121907
TITLE: Preparation of cocaine derivatives as an anti-cocaine
vaccine
INVENTOR(S): Wirsching, Peter; Janda, Kim D.
PATENT ASSIGNEE(S): Scripps Research Institute, USA; Wirsching, Peter;
Janda, Kim D.
SOURCE: PCT Int. Appl., 133 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9721451	A1	19970619	WO 1996-US19982	19961216
W: AU, CA, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2239058	AA	19970619	CA 1996-2239058	19961216
AU 9715658	A1	19970703	AU 1997-15658	19961216
AU 719289	B2	20000504		
EP 967993	A2	20000105	EP 1996-945392	19961216
R: DE, FR, GB, IT, NL				
US 6383490	B1	20020507	US 1998-77434	19980612
PRIORITY APPLN. INFO.:			US 1995-572849	A2 19951214
			WO 1996-US19982	W 19961216
OTHER SOURCE(S):		MARPAT 127:121907		

GI



AB Cocaine analogs, e.g. I, and their protein conjugates, are prepared for use as anticocaine vaccines. An anti-cocaine vaccine employs a cocaine hapten conjugated to a carrier protein. The anti-cocaine vaccine elicits an immune response which reduces the psychoactive effects of cocaine consumption by the production of anticocaine polyclonal **antibodies**. The **antibodies** may be employed in an ELISA test for assaying cocaine. The immune response elicited by the anti-cocaine vaccine produces **antibody** producing cells which may be isolated and cloned for producing anti-cocaine monoclonal **antibodies**.

IT 180633-51-6P

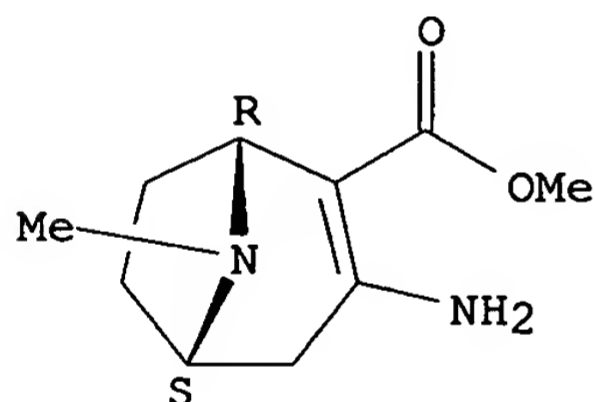
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of cocaine derivs. as an anticocaine vaccine)

RN 180633-51-6 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 3-amino-8-methyl-, methyl ester, (1R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:75293 CAPLUS

DOCUMENT NUMBER: 141:3203

TITLE: Substrate-assisted **antibody** catalysis

AUTHOR(S): Deng, Shixian; Bharat, Narine; de Prada, Paloma; Landry, Donald W.

CORPORATE SOURCE: Department of Medicine, Division of Clinical Pharmacology and Experimental Therapeutics, Columbia University, New York, NY, 10032, USA

SOURCE: Organic & Biomolecular Chemistry (2004), 2(3), 288-290
CODEN: OBCRAK; ISSN: 1477-0520

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 141:3203

AB A new strategy in transition-state analog design is demonstrated to elicit catalytic **antibodies**. The strategy is based on substrate-assisted **antibody** catalysis and utilizes analogs designed to mimic the transition-state for intramol. catalysis and thereby favor **antibodies** that can recruit catalytic groups from

substrate. The hydrolysis of the benzoyl ester of cocaine provides an illustration. The benzoyl ester of cocaine is distant from the protonated nitrogen in the stable chair conformer but proximate in the strained boat form. An **antibody** stabilizing the boat form and approximating ester and amine could catalyze ester hydrolysis. To mimic the transition-state for the intramol. catalysis, we synthesized a cocaine analog that replaces this ester with a methylenephosphinate bridge to the tropane nitrogen. This bridged analog elicited 85 cocaine esterases out of 450 anti-analog **antibodies**-a performance markedly superior to that of a simple phosphonate ester-based analog with an identical tether. The correspondence of the analog to a "high energy" conformer eliminated product inhibition. For certain polyfunctional targets, substrate assistance can be an effective strategy for eliciting catalytic **antibodies**.

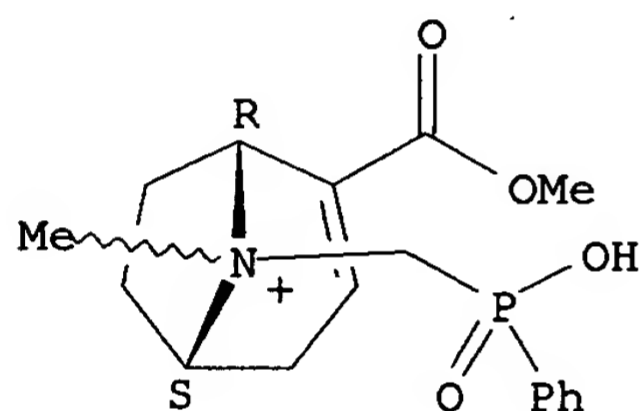
IT 697291-39-7

RL: FMU (Formation, unclassified); FORM (Formation, nonpreparative) (decomposition product; design of a transition state analog that elicits cocaine hydrolyzing **antibodies** as an example of substrate-assisted **antibody** catalysis)

RN 697291-39-7 CAPLUS

CN 8-Azoniabicyclo[3.2.1]oct-2-ene, 8-[(hydroxyphenylphosphinyl)methyl]-2-(methoxycarbonyl)-8-methyl-, iodide, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● I⁻

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1981:580646 CAPLUS

DOCUMENT NUMBER: 95:180646

TITLE: Cocaine radioimmunoassay - structure versus reactivity

AUTHOR(S): Budd, Robert D.

CORPORATE SOURCE: Los Angeles County Med. Examiner-Coroner, Los Angeles, CA, 90033, USA

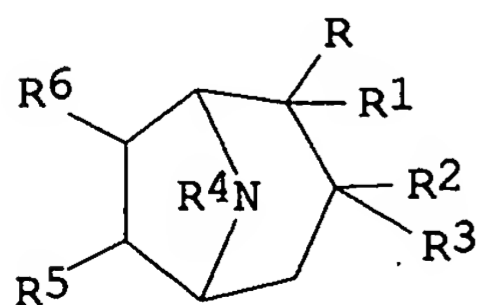
SOURCE: Clinical Toxicology (1981), 18(7), 773-82

CODEN: CTOXAO; ISSN: 0009-9309

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

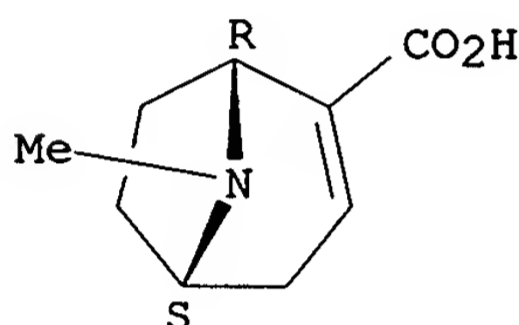
AB Cocaine [50-36-2] and 26 related compds. I (R and R1 = H, CO2H, CO2Me, etc.; R2 = H, OH, OBz; R3 = H, OH, OMe, aralkanoate, etc.; R4 = H, Me; R5 = H, OH, etc.; R6 = H, OH, etc.) were tested for Roche radioimmunoassay (RIA) benzoylecgonine **antibody**-binding activity. Benzoylecgonine [519-09-5] had the optimum **antibody**-binding activity; changes of any of the substituents (excepting esterification of the carboxylic acid group) reduced the binding. Cocaethylene (I; R = CO2Et, R1 = R3 = R5 = R6 = H, R2 = OBz, R4 = Me) [529-38-4] was the only drug which interfered with the Roche RIA of cocaine and its metabolites at therapeutic or overdose levels, but it is seldom encountered in therapeutic use or abuse. Thus, the Roche RIA studied is suitable for the anal. of urine samples for cocaine and its metabolites.

IT **484-93-5**
 RL: PROC (Process)
 (radioimmunoassay of, structure in relation to)

RN 484-93-5 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, (1R,5S)- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



=> d l11 ibib abs hitstr tot

L11 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:528117 CAPLUS

DOCUMENT NUMBER: 144:150506

TITLE: Development of polyfluorophenyltropanes: Potential probes for 19F magnetic resonance imaging (MRI) and spectroscopy (MRS) assessments of the dopamine transporter

AUTHOR(S): Zhang, Ao; Kula, Nora S.; Zhang, Kehong; Baldessarini, Ross J.; Kaufman, Marc J.; Renshaw, Perry F.; Neumeyer, John L.

CORPORATE SOURCE: Medicinal Chemistry Laboratory, Alcohol and Drug Abuse Research Center, Harvard Medical School, McLean Hospital, Belmont, MA, 02478-9106, USA

SOURCE: Letters in Drug Design & Discovery (2005), 2(4), 302-306
 CODEN: LDDDAW; ISSN: 1570-1808

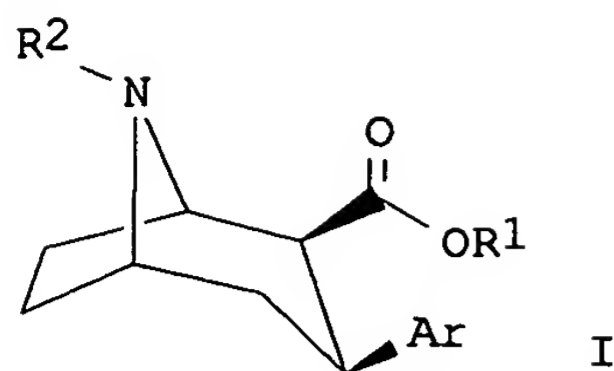
PUBLISHER: Bentham Science Publishers Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 144:150506

GI



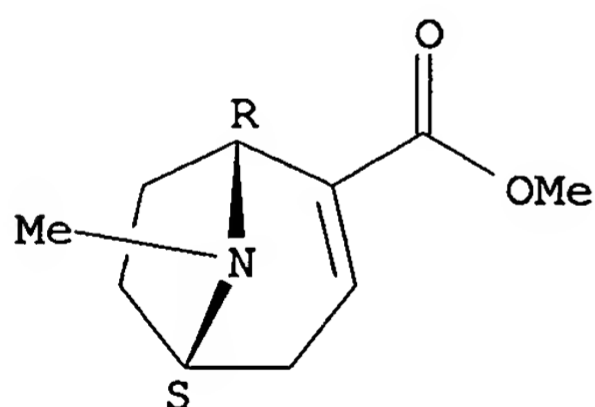
AB A novel series of nonradiolabeled, polyfluorinated phenyltropanes, e.g. I [Ar = Ph, C₆H₄CF₃-4, C₆H₃(CF₃)₂-3,5, C₆H₄(C₆H₄CF₃-4)-4, R₁ = R₂ = Me; Ar = C₆H₃(CF₃)₂-3,5, R₁ = Me, R₂ = H, (CH₂)₃F; Ar = C₆H₄I-4, R₁ = CH₂CF₃, R₂ = Me], were developed containing three or more ¹⁹F atoms/mol. in a magnetic resonance (MR) equivalent chemical environment to increase coherent MR signal characteristics. Competitive radioreceptor affinity assays of such compds. yielded nM affinity at dopamine (DAT) and serotonin (SERT) transporters in rat brain tissue. Compound I [Ar = C₆H₄CF₃-4, R₁ = R₂ = Me; (MCL-314)] at 50 μM gave a clear magnetic resonance spectroscopy signal, and I [Ar = C₆H₄I-4, R₁ = CH₂CF₃, R₂ = Me; (MCL-319)] yielded very high DAT potency and improved selectivity over SERT. Such compds. might potentially serve as MRI- or MRS-detectable index ligands for the dopamine transporter proteins, and preliminary observations call for further study of addnl. polyfluorinated phenyltropanes.

IT **43021-26-7P**, Anhydroecgonine methyl ester
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and stereoselective **conjugate** addition to, by polyfluorinated aryl Grignards; development of polyfluorophenyltropanes as potential probes for ¹⁹F magnetic resonance imaging and spectroscopy)

RN 43021-26-7 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, methyl ester, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:997722 CAPLUS

DOCUMENT NUMBER: 142:280328

TITLE: Ab initio mo calculation studies for several novel entries to tropane compounds

AUTHOR(S): Forsythe, Kelsey M.; Robertson, Daniel H.; Zheng, Qi-Huang

CORPORATE SOURCE: Department of Chemistry, Indiana University Purdue University at Indianapolis, Indianapolis, IN, 46202, USA

SOURCE: Journal of Theoretical & Computational Chemistry (2004), 3(3), 305-323

CODEN: JTCCAC; ISSN: 0219-6336

PUBLISHER: World Scientific Publishing Co. Pte. Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Tropane alkaloids are generally known as anticholinergics. Radiolabeled tropane compds. could be brain imaging agents used in biomedical imaging technique positron emission tomog. (PET). A novel entry to aryltropane analogs of cocaine was developed based on the **conjugate** addition reaction of Grignard reagents phenylmagnesium, (4'-isopropenylphenyl)magnesium, or 2-naphthylmagnesium bromide to α,β -unsatd. esters anhydroecgonine Me ester, or t-Bu ester, which gave several aryltropans with high binding affinities for dopamine and serotonin transporters. Basic conditions are frequently employed in the radiolabeling chemical of many aryltropane cocaine analogs. However, isomerization at C-2 position can also occur under basic conditions, resulting in loss of the biol. potent 2 β -isomers by conversion to the much less active 2 α -isomer. Tropinone could be envisaged as a convenient starting material for the synthesis of diverse tropane alkaloids. A novel entry into tropane alkaloid intermediates was developed based on the ring-opening reaction of tropinone. In this reaction, the enolate of tropinone, resulting from deprotonation with lithium diisopropylamide [LDA, LiN(CHMe₂)₂] or sodium bis(trimethylsilyl)amide [NaN(SiMe₃)₂] was treated with alkyl chloroformate to give a novel, structurally unique class of tropane alkaloid intermediates 6-N-carboalkoxy-N-methyl-2-cycloheptenone, 1-alkyoxycarboxy-6-N-carboalkoxy-N-methyl-2,7-cyclohept-dien and 6-N-carboalkoxy-N-methyl-7-carboalkoxy-2,7-cyclohept-dien-ol. In this paper the **conjugate** addition reaction of Grignard reagents to α,β -unsatd. esters, the isomerization of aryltropane cocaine analogs, and the ring-opening reaction of tropinone by ab initio MO calcn. at the Hartree-Fock (HF) level. is studied. The calcn. results solely in terms of energetics indicate that the 2 α -isomers (equatorial configurations) of aryltropane cocaine analogs are more stable than their 2 β -isomers (axial configurations), at the AM1, STO-3G and 3-21G(*) levels, and the Grignard 1,4- and then 1,2-addition (double addition) products are likely more stable than the Grignard 1,4-addition (single addition) products, at the STO-3G and 3-21G(*) levels except at the AM1 level. Therefore the tendency of Grignard addition toward double addition is competitive with single addition, and the isomerization tends to the formation of more stable 2 α -isomers. Likewise, the calcn. results solely in terms of energetics indicate that the stability of the reaction product forms at the AM1, STO-3G and 3-21G(*) levels, and the tendency of alkyl chloroformate addition toward double addition to the products is competitive with single addition to the products. Ab initio MO calcns. provide a theor. rationalization for the chemoselectivity of the **conjugate** addition reaction and the ring-opening reaction, the most stable configurations of reaction products, and the isomerization.

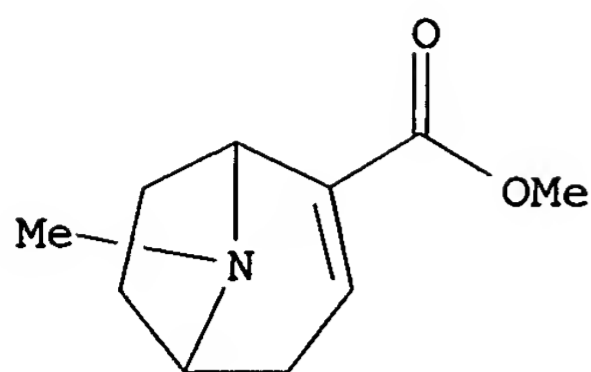
IT 127379-24-2 847487-91-6

RL: RCT (Reactant); RACT (Reactant or reagent)

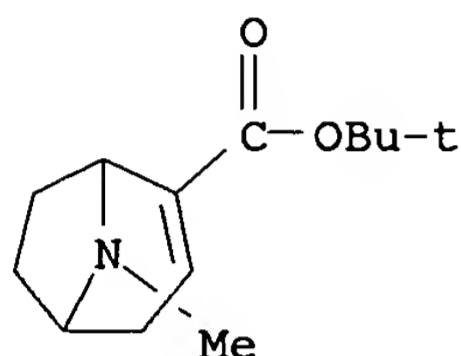
(ab initio mo calcn. studies for several novel entries to tropane compds. including Grignard **conjugate** addition, isomerization, and ring-opening products)

RN 127379-24-2 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, methyl ester (9CI) (CA INDEX NAME)



RN 847487-91-6 CAPLUS
 CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-,
 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:956779 CAPLUS

DOCUMENT NUMBER: 142:411512

TITLE: Synthesis of stereoisomers of 6 β - and
 7 β -(benzylthio)-3-(p-tolyl) tropane-2-carboxylic
 acid methyl ester

AUTHOR(S): Masri, Fadi; Riche, Francoise; Durif, Andre; Philouze,
 Christian; Vallee, Yannick

CORPORATE SOURCE: Laboratoire d'Etudes Dynamiques et Structurales de la
 Selectivite, Institut de Chimie Moleculaire de
 Grenoble, Universite Joseph Fourier Grenoble I,
 Grenoble, 38041, Fr.

SOURCE: Journal of Sulfur Chemistry (2004), 25(4), 259-268
 CODEN: JSCOF; ISSN: 1741-5993

PUBLISHER: Taylor & Francis Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 142:411512

AB To develop new ^{99m}Tc-labeled agents to evaluate dopamine transporters
 (DAT) involved in Parkinson's disease, by in vivo SPECT imaging, we have
 synthesized six new sulfur-containing ligands with the tropane skeleton. We
 have introduced the complexing sulfur atom far from the three sites of
 recognition by DAT of these tropane derivs. The 6 β -substituted
 tropinone has been obtained by a double Mannich condensation followed by
 the introduction of the moieties for mol. interactions at the binding site
 on C2 and C3, leading to the six stereoisomers.

IT **848590-43-2P 848590-44-3P**

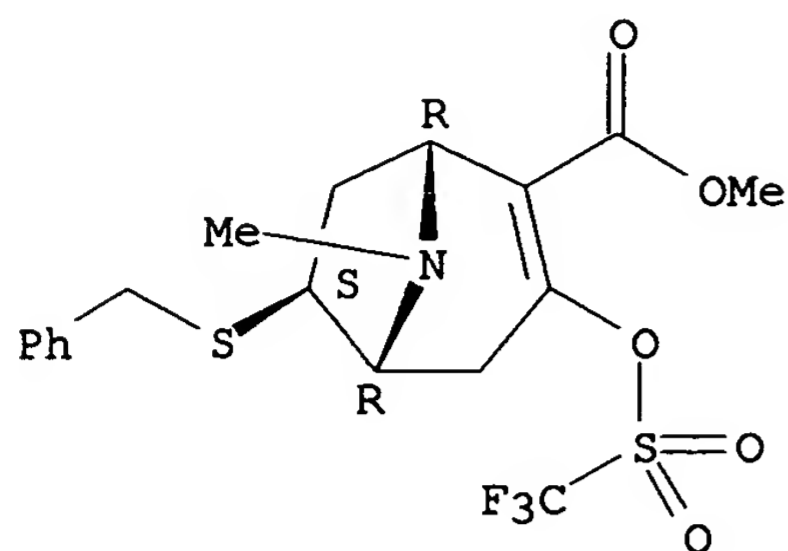
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)

(preparation and palladium-catalyzed coupling of, with tolylboronic acid;
 synthesis of stereoisomers of 6 β - and 7 β -(benzylthio)-3-(p-
 tolyl) tropane-2-carboxylic acid Me ester)

RN 848590-43-2 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-6-
 [(phenylmethyl)thio]-3-[[trifluoromethyl)sulfonyl]oxy]-, methyl ester,
 (1R,5R,6S)-rel- (9CI) (CA INDEX NAME)

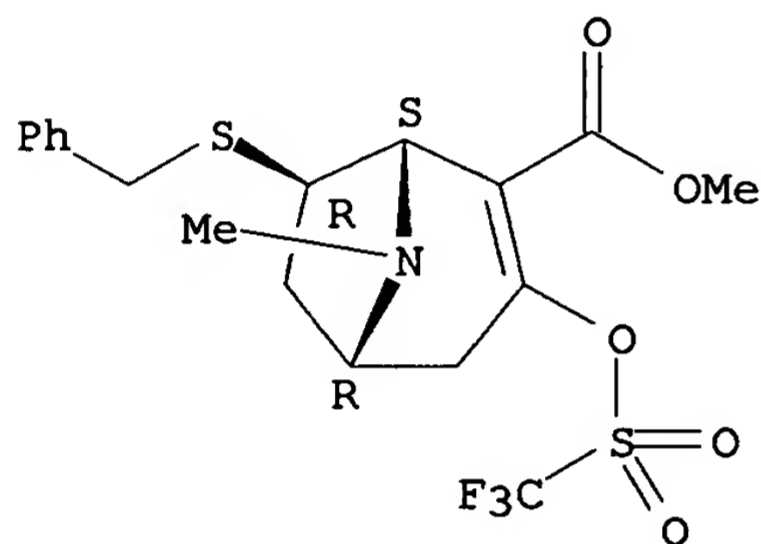
Relative stereochemistry.



RN 848590-44-3 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-7-[(phenylmethyl)thio]-3-[[trifluoromethyl)sulfonyl]oxy]-, methyl ester, (1R,5S,7S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 848590-46-5P 848590-47-6P

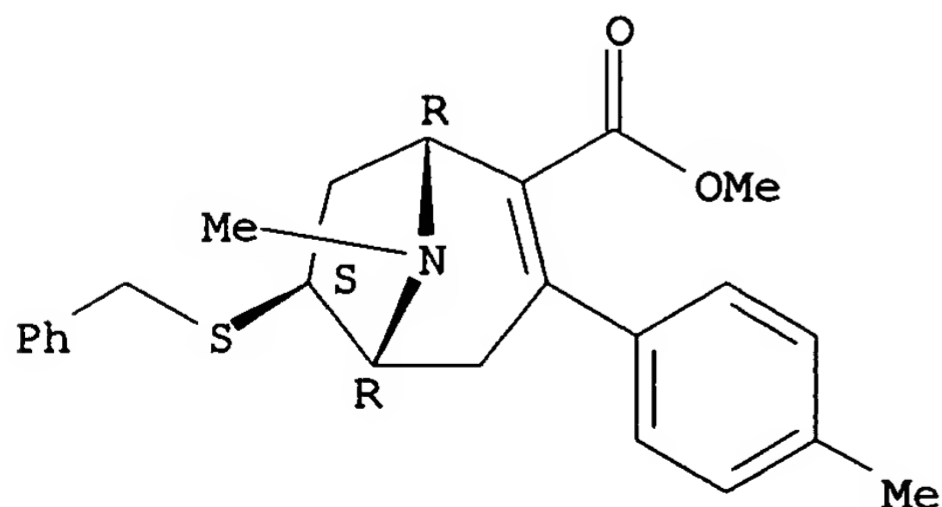
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation, crystal structure and **conjugate** reduction of, with samarium iodide; synthesis of stereoisomers of 6 β - and 7 β -(benzylthio)-3-(p-tolyl) tropane-2-carboxylic acid Me ester)

RN 848590-46-5 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-3-(4-methylphenyl)-6-[(phenylmethyl)thio]-, methyl ester, (1R,5R,6S)-rel- (9CI) (CA INDEX NAME)

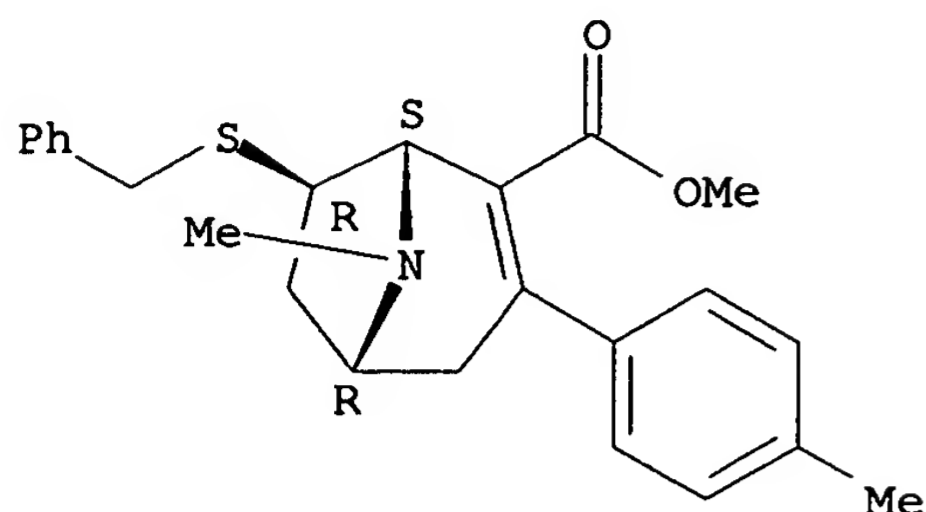
Relative stereochemistry.



RN 848590-47-6 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-3-(4-methylphenyl)-7-[(phenylmethyl)thio]-, methyl ester, (1R,5S,7S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:344208 CAPLUS

DOCUMENT NUMBER: 141:71743

TITLE: Two- and Three Dimensional Combinatorial Chemistry from Multicomponent Grignard Reagents

AUTHOR(S): Buelow, Anne; Sinning, Steffen; Wiborg, Ove; Bols, Mikael

CORPORATE SOURCE: Department of Chemistry, University of Aarhus, Aarhus, DK-8000, Den.

SOURCE: Journal of Combinatorial Chemistry (2004), 6(4), 509-519

CODEN: JCCHFF; ISSN: 1520-4766

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The **conjugate** addition of five component Grignard reagents to Me ecgonidine was used to create libraries of 3-substituted tropanes. By variation in the reagent combination in 10 such 5-membered sublibraries, a library of 25 compds. was made in a two-dimensional format. Screening of this library led to identification of two new potent monoamine transporter ligands that were subsequently synthesized. The most potent compound in this library was (1R,2S,3S,5S)-3-(3,4-dimethylphenyl)-8-methyl-8-azabicyclo[3.2.1]octane-2-carboxylic acid Me ester, which inhibited dopamine transporter (hDAT) binding and reuptake with a K_i of 26 and 20 nM, resp. The **conjugate** addition to a 5-membered library of Me ecgonidine analogs with variation of nitrogen substituent was also carried out and used to create 15 sublibraries of 25 compds., which displayed 125 compds. in a three-dimensional format. From this 3D library, several potent dopamine transport inhibitors were likewise identified and synthesized. The most potent hDAT inhibitor discovered was (1R,2S,3S,5S)-3-(3,4-dimethylphenyl)-8-pentyl-8-azabicyclo[3.2.1]octane-2-carboxylic acid Me ester. The study also showed that 3-alkyltropanes were poor inhibitors of monoamine transporters.

IT 43021-26-7

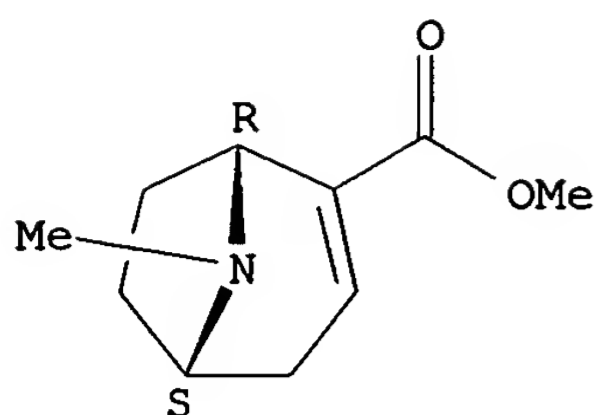
RL: CRT (Combinatorial reactant); RCT (Reactant); CMBI (Combinatorial study); RACT (Reactant or reagent)

(preparation of two and three dimensional combinatorial libraries of tropanes via Grignard **conjugate** addition and activity as monoamine transporter inhibitors)

RN 43021-26-7 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, methyl ester, (1R,5S)- (9CI) (CA INDEX NAME)

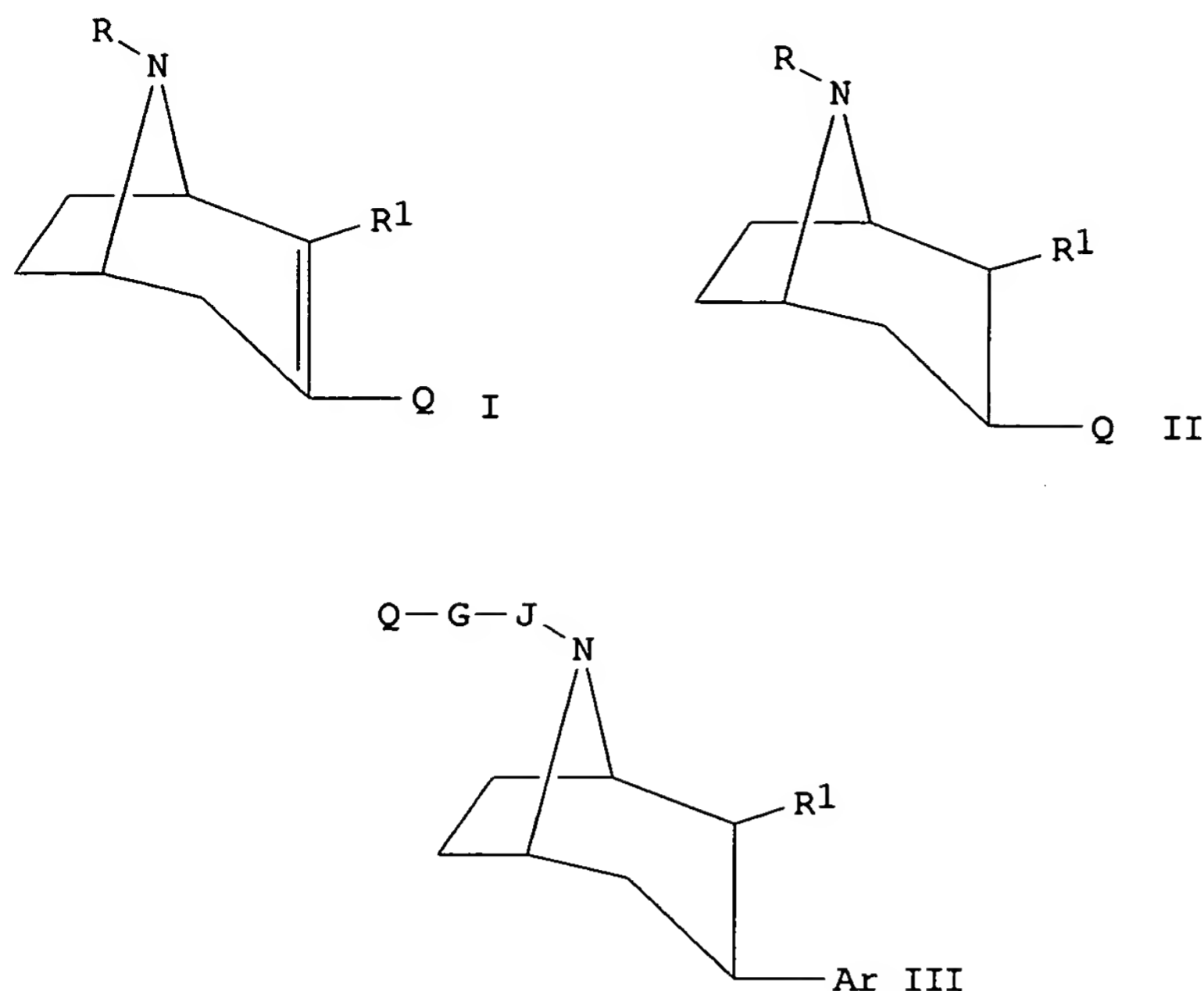
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2001:416949 CAPLUS
 DOCUMENT NUMBER: 135:33571
 TITLE: Transition metal-cyclopentadienyl-tropane
conjugates with affinity for monoamine
 transporters, their preparation and use as diagnostic
 or therapeutic agents
 INVENTOR(S): Tamagnan, Gilles Denis; Baldwin, Ronald Martin; Innis,
 Robert B.
 PATENT ASSIGNEE(S): Yale University, USA
 SOURCE: PCT Int. Appl., 45 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001040239	A2	20010607	WO 2000-US42447	20001201
WO 2001040239	A3	20001227		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2393610	AA	20010607	CA 2000-2393610	20001201
US 2002111486	A1	20020815	US 2000-727076	20001201
EP 1233968	A2	20020828	EP 2000-992372	20001201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003515541	T2	20030507	JP 2001-540994	20001201
PRIORITY APPLN. INFO.:			US 1999-168671P	P 19991203
			WO 2000-US42447	W 20001201
OTHER SOURCE(S):		MARPAT 135:33571		
GI				



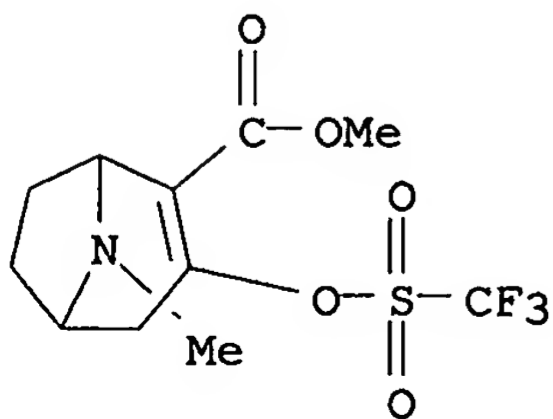
AB Transition metal-cyclopentadienyl-tropane **conjugate** compds., e.g., I, II [$\text{R}^1 = \text{CO}_2\text{R}_2$, CH_2OR_2 ; R , $\text{R}_2 = \text{H}$, (un)branched C1-12 alkyl, C2-12 alkenyl, C2-12 alkynyl, C6-12 aryl, C3-12 cycloalkyl, C3-12 heterocycloalkyl, C1-12 heteroarom. group wherein the heteroatom is N, O or S; $\text{Q} = (\text{un})\text{substituted CpM}(\text{CO})_3$; $\text{M} = \text{Re}$, Tc , Mn or radioisotope; $\text{Cp} = \text{cyclopentadienyl}$] or III [$\text{Q} = (\text{un})\text{substituted CpM}(\text{CO})_3$, same M , Cp ; $\text{G} = \text{direct link}$, CO , R_2NCO , $\text{CH}:\text{CH}$, $\text{C}(\text{O})$, SO_2 , O_2C , $\text{CH}_2\text{O}(\text{CH}_2)_r\text{O}(\text{CH}_2)_s$; $r = 1-4$, $s = 0-4$, where $r + s < 8$; $\text{J} = (\text{CH}_2)_n$, $n = 1-8$; same R^1 ; $\text{Ar} = (\text{un})\text{substituted Ph}$ group; when $\text{R}^1 = \text{CO}_2\text{Me}$ or CH_2OH , $\text{G} \neq \text{CO}$] useful as radiodiagnostic agents (no data) or as diagnostic or therapeutic agents for treatment of disorders related to monoamine transporter activity, such as clin. diagnosis of Parkinson's disease, are claimed, as are methods for their preparation. In an example, the binding affinity K_i of III [$\text{R}^1 = \text{CO}_2\text{Me}$, $\text{Ar} = 4\text{-ClC}_6\text{H}_4$, $\text{J} = (\text{CH}_2)_3$, $\text{G} = \text{O}_2\text{C}$, $\text{Q} = \text{CpRe}(\text{CO})_3$; preparation given] for dopamine transporter (DAT) was 4.18 ± 0.33 nM, for serotonin transporter (5-HTT) was 5.28 ± 0.21 nM and for norepinephrine transporter (NET) was 74.0 ± 8.2 nM.

IT **343612-72-6**

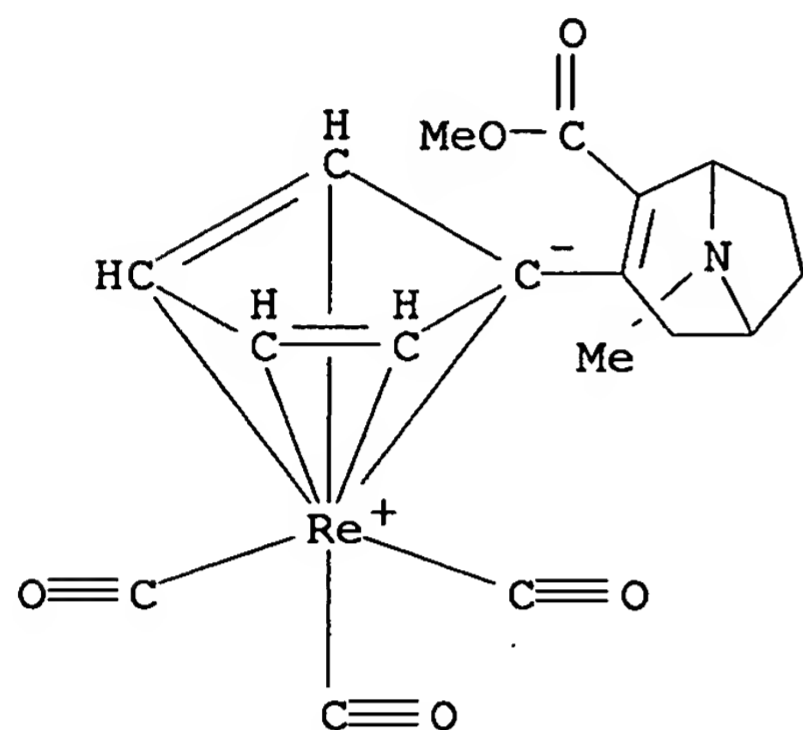
RL: RCT (Reactant); RACT (Reactant or reagent)
 (catalytic coupling reaction of, with [(trimethylstannyl)cyclopentadienyl]rhenium tricarbonyl)

RN 343612-72-6 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-3-[[[(trifluoromethyl)sulfonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)



IT 343612-70-4P
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process) (preparation and binding affinity for dopamine, serotonin and norepinephrine transporters)
 RN 343612-70-4 CAPLUS
 CN Rhenium, tricarbonyl[(1,2,3,4,5-η)-1-[2-(methoxycarbonyl)-8-methyl-8-azabicyclo[3.2.1]oct-2-en-3-yl]-2,4-cyclopentadien-1-yl]- (9CI) (CA INDEX NAME)



L11 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1998:512816 CAPLUS
 DOCUMENT NUMBER: 129:199620
 TITLE: Cocaine Benzoyl Thioester: Synthesis, Kinetics of Base Hydrolysis, and Application to the Assay of Cocaine Esterases
 AUTHOR(S): Cashman, John R.; Berkman, Clifford E.; Underiner, Gail; Kolly, Carrie A.; Hunter, Allen D.
 CORPORATE SOURCE: Human BioMolecular Research Institute, Seattle, WA, 98199, USA
 SOURCE: Chemical Research in Toxicology (1998), 11(8), 895-901
 CODEN: CRTOEC; ISSN: 0893-228X
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The synthesis and characterization of diastereomers of cocaine benzoyl thioester is described. Allococaine benzoyl thioester and allopseudococaine benzoyl thioester were synthesized by the conjugate addition of p-methoxytolyl thiol to ecgonine Me ester followed by debenzoylation and benzoylation. The absolute structure of the hydrochloride salt of the major ecgonine p-methoxytolyl sulfide formed was determined by single-crystal diffraction anal. and used to establish the addition geometry. When placed in aqueous solution, the cocaine benzoyl thioester diastereomers hydrolyzed to give thioecgonine Me ester. The rate of cocaine benzoyl thioester hydrolysis was carefully investigated spectrophotometrically by using the Ellman reagent. At neutral pH, the hydrolysis of the diastereomers was found to proceed at detectable rates. Upon increasing pH, the rate of hydrolysis of cocaine benzoyl thioester diastereomers was increased and the reaction was catalyzed by basic buffer species. In addition to defining the kinetics of hydrolysis in aqueous solution, cocaine benzoyl thioester was utilized as a highly efficient method to

monitor the activity of cholinesterases and pig liver esterase. Use of cocaine benzoyl thioester represents a rapid and sensitive way to screen for cocaine esterase activity.

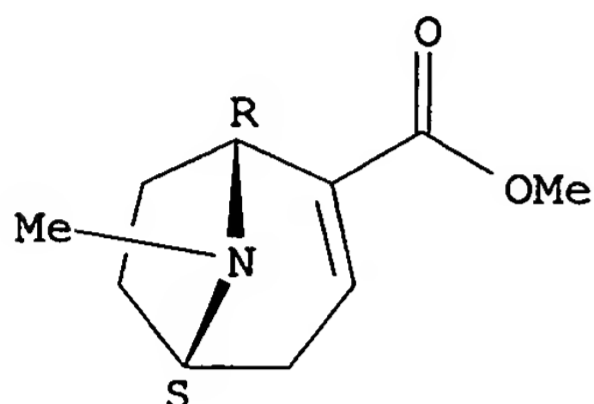
IT 43021-26-7

RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis, kinetics of base hydrolysis, and application to assay of cocaine esterases of cocaine benzoyl thioester)

RN 43021-26-7 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, methyl ester, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:81529 CAPLUS

DOCUMENT NUMBER: 126:171741

TITLE: Stereoselective synthesis of 2 β -carbomethoxy-3 β -phenyltropane derivatives. Enhanced stereoselectivity observed for the **conjugate** addition reaction of phenylmagnesium bromide derivatives with anhydrous dichloromethane

AUTHOR(S): Xu, Lifan; Trudell, Mark L.

CORPORATE SOURCE: Dep. Chem., Univ. New Orleans, New Orleans, LA, 70148, USA

SOURCE: Journal of Heterocyclic Chemistry (1996), 33(6), 2037-2039

CODEN: JHTCAD; ISSN: 0022-152X

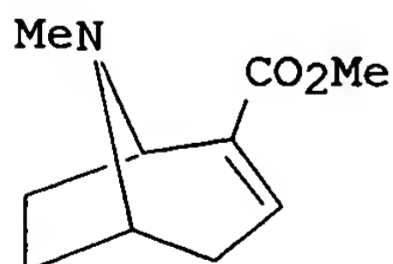
PUBLISHER: HeteroCorporation

DOCUMENT TYPE: Journal

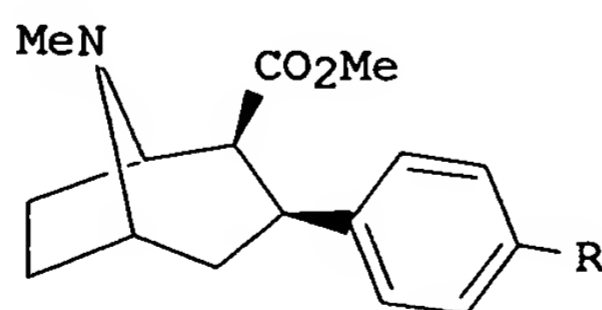
LANGUAGE: English

OTHER SOURCE(S): CASREACT 126:171741

GI



I



II

AB The use of dichloromethane as a solvent for the **conjugate** addition reaction of preformed ethereal solns. of phenylmagnesium bromide derivs. with anhydroecgonine Me ester (I) was found to enhance the stereoselectivity of the reaction and provide the 2 β -carbomethoxy-3 β -phenyltropane derivs. II (R = H, Me, Cl, F) in high yield.

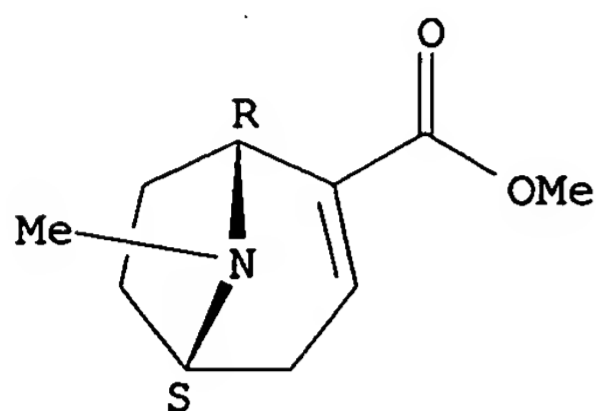
IT 43021-26-7, (-)-Anhydroecgonine methyl ester

RL: RCT (Reactant); RACT (Reactant or reagent)
(stereoselective **conjugate** addition of phenylmagnesium bromide
derivs. to anhydroecgonine ester)

RN 43021-26-7 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, methyl ester,
(1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:47794 CAPLUS

DOCUMENT NUMBER: 126:131673

TITLE: Improved synthesis of β -CIT and [^{11}C] β -CIT
labeled at nitrogen or oxygen positions

AUTHOR(S): Zheng, Qi-Huang; Mulholland, G. Keith

CORPORATE SOURCE: SCHOOL MEDICINE, INDIANA UNIVERSITY, Indianapolis, IN,
46202-5121, USA

SOURCE: Nuclear Medicine and Biology (1996), 23(8), 981-986
CODEN: NMBIEO; ISSN: 0883-2897

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The important radiotracer precursor 2 β -carbomethoxy-3 β -(4-
idophenyl)-tropane (β -CIT, RTI-55) was made in 52% overall yield from
cocaine. Key steps were improved **conjugate** Grignard addition to
anhydroecgonine Me ester with >3.5:1 2 β : 2 α -isomer selectivity,
and a mild new direct aromatic iodination with I₂ and silver triflate in
CH₂Cl₂. The [^{11}C] β -CIT was labeled at either the N or O positions
with [^{11}C]methyl triflate; and efficient reversed-phase HPLC was used to
preparatively sep. [N- ^{11}C] β -CIT from N-nor- β -CIT for the first
time, and a fast solid-phase extraction (SPE) method was applied to
preparatively sep. [O- ^{11}C] β -CIT from β -CIT-acid precursor.

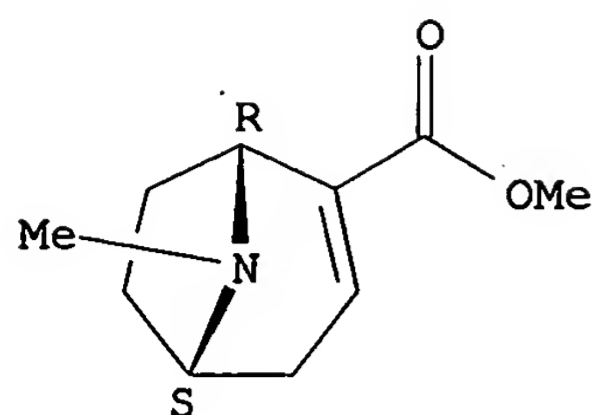
IT 43021-26-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(synthesis of labeled iodophenyltropanes for use as imaging tools for
neuronal monoamine uptake)

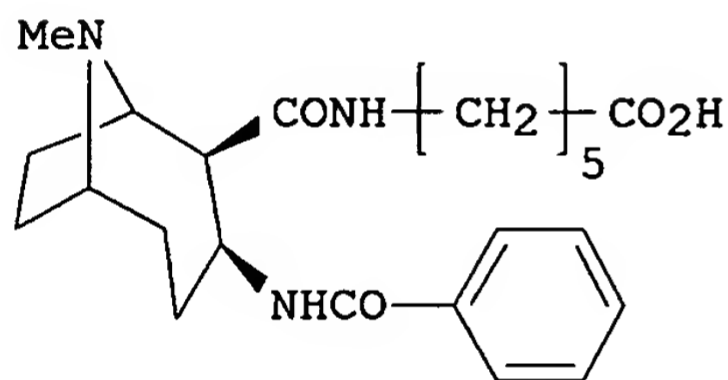
RN 43021-26-7 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, methyl ester,
(1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L11 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1996:477579 CAPLUS
 DOCUMENT NUMBER: 125:196066
 TITLE: Design and synthesis of a cocaine-diamide
hapten for vaccine development
 AUTHOR(S): Sakurai, Mitsuya; Wirsching, Peter; Janda, Kim D.
 CORPORATE SOURCE: Departments of Molecular Biology and Chemistry, The
 Scripps Research Institute, La Jolla, CA, 92037, USA
 SOURCE: Tetrahedron Letters (1996), 37(31), 5479-5482
 CODEN: TELEAY; ISSN: 0040-4039
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



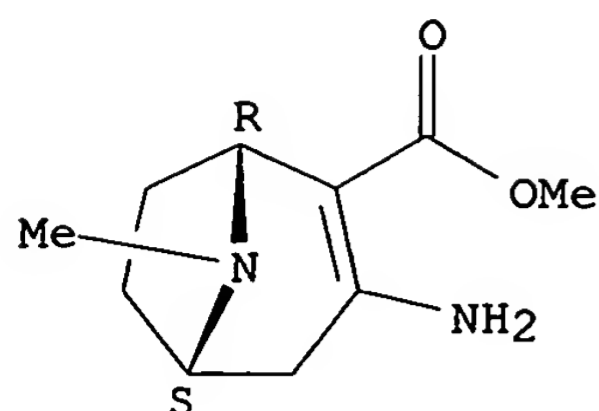
I

AB A cocaine-diamide **hapt**en was designed in an effort to obtain a potent, long-lasting anti-cocaine immune response for the treatment of cocaine abuse. The analog incorporated an amido linker functionality in place of the carbomethoxy group at C-2 and a benzoylamino replacement of the benzoyloxy group at C-3 of the cocaine framework. Diamide I was synthesized in 6 steps starting from (+)-2 β -carbomethoxy-3-tropinone.

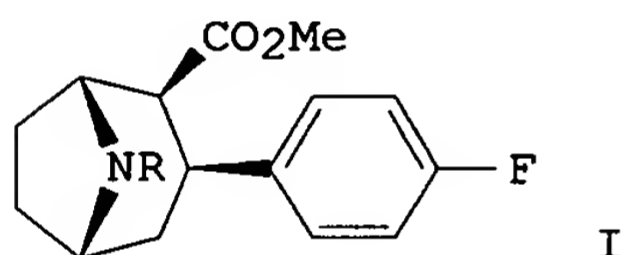
IT **180633-51-6P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (design and synthesis of a cocaine-diamide **hapt**en for vaccine development)

RN 180633-51-6 CAPLUS
 CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 3-amino-8-methyl-, methyl ester, (1R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1991:221151 CAPLUS
 DOCUMENT NUMBER: 114:221151
 TITLE: Synthesis and receptor binding of N-substituted tropane derivatives. High-affinity ligands for the cocaine receptor
 AUTHOR(S): Milius, Richard A.; Saha, Jayanta K.; Madras, Bertha K.; Neumeyer, John L.
 CORPORATE SOURCE: Res. Biochem. Inc., Natick, MA, 01760, USA
 SOURCE: Journal of Medicinal Chemistry (1991), 34(5), 1728-31
 CODEN: JMCMAR; ISSN: 0022-2623
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 114:221151
 GI



AB The synthesis and pharmacol. characterization of a series of N-substituted 3-(4-fluorophenyl)tropane derivs. (I; R = Me, H, CH₂CH:CH₂, Pr) is reported. The compds. displayed binding characteristics that paralleled those of cocaine, and several had substantially higher affinity at cocaine recognition sites. **Conjugate** addition of 4-fluorophenylmagnesium bromide to anhydroecgonine Me ester gave I (R = Me) (WIN 35,428) (II) after flash chromatog. II, the most potent analog, was tritiated at a specific activity of 81.3 Ci/mmol. The labeled compound was bound rapidly and reversibly to caudate putamen membranes; the two-component binding curve typical of cocaine analogs was observed Equilibrium was achieved within

2 h

and was stable for at least 4 h. High- and low-affinity K_d values observed for [3H]-II (4.7 and 60 nM, resp.) were more than 4 times lower than those for [3H]cocaine, and the d. of binding sites [B_{max} = 50 pmol/g, high, and 290 pmol/g, low) for the two drugs were comparable. Nonspecific binding of [3H]-II was 5-10% of total binding.

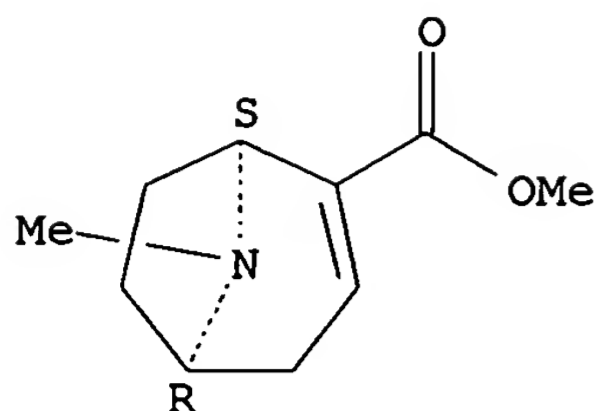
IT 50373-10-9

RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, with fluorophenylmagnesium bromide)

RN 50373-10-9 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, methyl ester, (1S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L11 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1923:9281 CAPLUS

DOCUMENT NUMBER: 17:9281

ORIGINAL REFERENCE NO.: 17:1643i,1644a-c

TITLE: The spectrochemistry of derivatives of tropane

AUTHOR(S): von Auwers, K.

SOURCE: Journal fuer Praktische Chemie (Leipzig) (1922), 105, 102-19

CODEN: JPCEAO; ISSN: 0021-8383

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB Extensive data are given of the optical properties of the following compds.: tropane, tropidine, tropine, acetyltropeine, propionyltropeine, tropinone, Et tropane-2-carboxylate, Et tropidine-2-carboxylate, Me l-ecgonine, Et tropinone-2-carboxylate, tropacocaine, d-ψ-cocaine, dl ψ-cocaine, ψ-pelletierine, di-Et N-methylpyrrolidine-2,5-diacetate, 2,4,6-trimethylpiperidine, N-methyl-24,6- trimethylpiperidine (prepared by boiling copellidine and MeI, diluting with H₂O, filtering, making alkaline with NaOH, extracting with Et₂O, drying over KOH and distilling, b. 153-5°, d₄²⁰ 0.823). N-methyltetrahydroquinoline, bornyl acetate, isobornyl acetate, bornyl isovalerate, N-methylcamphidine, (prepared by rubbing camphidine with MeI, diluting with a little HO₂, adding NaOH, extracting with Et₂O, drying over KOH and distilling, oil with an odor of camphor, b. 195-7°, slightly soluble in H₂O with strong alkaline reaction, gives a precipitate with HgCl₂ and H₂PtCl₆ (picrate, short fine needles from hot H₂O, m.

234°)). The data include at various temps. d₄t, n_Dt, n_Dt, n_Dt, M_D, M_D M_D-M_D, M_D-M_D EMD, EMD-EMD, EMD-EMD, EMD, EMD, beta.-Σα, EΣγ-Σα and ED₂O. The first 8 compds. show depressions of the sp. refraction and dispersion which with slight deviations have average values of EΣrefr. = -0.5 and EΣdisp. = -9%. The next 5 compds. do not have such depressions, but only because the latter are masked by other influences, such as a conjugate system. The spectrochem. values of ψ/-pelletierine are similar to tropane, though structurally different. The next 5 compds. are normal, the next 3 anomalous, and the last 5 normal. Compds. containing a 7-or 8-membered ring with a =NMe group as a bridge are characterized by a spectrochem. anomaly.

IT 137331-56-7, Tropidine-2-carboxylic acid, ethyl ester (optical properties of)

RN 137331-56-7 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, ethyl ester (9CI) (CA INDEX NAME)